hypermanganesemia with dystonia, polycythemia, and cirrhosis

Hypermanganesemia with dystonia, polycythemia, and cirrhosis (HMDPC) is an inherited disorder in which excessive amounts of the element manganese accumulate in the body, particularly in the brain, liver, and blood (hypermanganesemia). Signs and symptoms of this condition can appear in childhood (early-onset), typically between ages 2 and 15, or in adulthood (adult-onset).

Manganese accumulates in a region of the brain responsible for the coordination of movement, causing neurological problems that make controlling movement difficult. Most children with the early-onset form of HMDPC experience involuntary tensing of the muscles in the arms and legs (four-limb dystonia), which often leads to a characteristic high-stepping walk described as a "cock-walk gait." Other neurological symptoms in affected children include involuntary trembling (tremor), unusually slow movement (bradykinesia), and slurred speech (dysarthria). The adult-onset form of HMDPC is characterized by a pattern of movement abnormalities known as parkinsonism, which includes bradykinesia, tremor, muscle rigidity, and an inability to hold the body upright and balanced (postural instability).

Affected individuals have an increased number of red blood cells (polycythemia) and low levels of iron stored in the body. Additional features of HMDPC can include an enlarged liver (hepatomegaly), scarring (fibrosis) in the liver, and irreversible liver disease (cirrhosis).

Frequency

The prevalence of HMDPC is unknown. A small number of cases have been described in the scientific literature.

Genetic Changes

Mutations in the *SLC30A10* gene cause HMDPC. This gene provides instructions for making a protein that transports manganese across cell membranes. Manganese is important for many cellular functions, but large amounts are toxic, particularly to brain and liver cells. The SLC30A10 protein is found in the membranes surrounding liver cells and nerve cells in the brain, as well as in the membranes of structures within these cells. The protein protects these cells from high concentrations of manganese by removing manganese when levels become elevated.

Mutations in the *SLC30A10* gene impair the transport of manganese out of cells, allowing the element to build up in the brain and liver. Manganese accumulation in

the brain leads to the movement problems characteristic of HMDPC. Damage from manganese buildup in the liver leads to liver abnormalities in people with this condition. High levels of manganese help increase the production of red blood cells, so excess amounts of this element also result in polycythemia.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- dystonia/parkinsonism, hypermanganesemia, polycythemia, and chronic liver disease
- hepatic cirrhosis, dystonia, polycythaemia, and hypermanganesaemia
- hepatic cirrhosis, dystonia, polycythemia, and hypermanganesemia
- HMDPC
- parkinsonism and dystonia with hypermanganesemia, polycythemia, and chronic liver disease

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Hypermanganesemia with dystonia, polycythemia and cirrhosis
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2750442/

Other Diagnosis and Management Resources

- GeneReview: Dystonia/Parkinsonism, Hypermanganesemia, Polycythemia, and Chronic Liver Disease
  https://www.ncbi.nlm.nih.gov/books/NBK100241

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html

- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Cirrhosis
  https://medlineplus.gov/cirrhosis.html
- Health Topic: Dystonia
  https://medlineplus.gov/dystonia.html
- Health Topic: Movement Disorders
  https://medlineplus.gov/movementdisorders.html
- Health Topic: Neurologic Diseases
  https://medlineplus.gov/neurologicdiseases.html

Genetic and Rare Diseases Information Center

- Hypermanganesemia with dystonia polycythemia and cirrhosis
  https://rarediseases.info.nih.gov/diseases/10706/hypermanganesemia-with-dystonia-polycythemia-and-cirrhosis

Additional NIH Resources

- National Digestive Diseases Information Clearinghouse: Cirrhosis
  https://www.niddk.nih.gov/health-information/liver-disease/cirrhosis
- National Institute of Neurological Disorders and Stroke: Dystonias Fact Sheet
  https://www.ninds.nih.gov/Disorders/All-Disorders/Dystonias-Information-Page

Educational Resources

- Agency for Toxic Substances and Disease Registry: Manganese
  https://www.atsdr.cdc.gov/toxfaqs/tf.asp?id=101&tid=23
- Dystonia Medical Research Foundation: What is Dystonia?
  https://www.dystonia-foundation.org/what-is-dystonia
- MalaCards: hypermanganesemia with dystonia, polycythemia, and cirrhosis
  http://www.malacards.org/card/hypermanganesemia_with_dystonia_polycythemia_and_cirrhosis_2

- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Dystonia/Parkinsonism,%20Hypermanganesemia,%20Polycythemia,%20and%20Chronic%20Liver%20disease&type=profile
- Oregon State University Linus Pauling Institute: Manganese
  http://lpi.oregonstate.edu/mic/minerals/manganese

Patient Support and Advocacy Resources

- American Liver Foundation
  http://www.liverfoundation.org/

GeneReviews

- Dystonia/Parkinsonism, Hypermanganesemia, Polycythemia, and Chronic Liver Disease
  https://www.ncbi.nlm.nih.gov/books/NBK100241

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28parkinsonism/dystonia,+polycythemia,+chronic+liver+disease%29+OR+%28hepatic+cirrhosis,+dystonia,+polycythemia+and+hypermanganesemia%29+OR+%28hypermanganesemia%29+AND+%28dystonia%29+OR+%28hypermanganesaemia%29%29+AND+english%5Bla%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- HYPERMANGANESEMIA WITH DYSTONIA 1
  http://omim.org/entry/613280

Sources for This Summary

- GeneReview: Dystonia/Parkinsonism, Hypermanganesemia, Polycythemia, and Chronic Liver Disease
  https://www.ncbi.nlm.nih.gov/books/NBK100241
- Quadri M, Federico A, Zhao T, Breedveld GJ, Battisti C, Delnooz C, Severijnen LA, Di Toro Mammarella L, Mignarri A, Monti L, Sanna A, Lu P, Punzo F, Cossu G, Willemsen R, Rasi F, Oostra BA, van de Warrenburg BP, Bonifati V. Mutations in SLC30A10 cause parkinsonism and dystonia with hypermanganesemia, polycythemia, and chronic liver disease. Am J Hum Genet. 2012 Mar 9; 90(3):467-77. doi: 10.1016/j.ajhg.2012.01.017. Epub 2012 Feb 16.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22341971
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3309204/

- Tuschl K, Clayton PT, Gospe SM Jr, Gulab S, Ibrahim S, Singhi P, Aulakh R, Ribeiro RT, Barsottini OG, Zaki MS, Del Rosario ML, Dyack S, Price V, Rideout A, Gordon K, Wevers RA, Chong WK, Mills PB. Syndrome of hepatic cirrhosis, dystonia, polycythemia, and hypermanganesemia caused by mutations in SLC30A10, a manganese transporter in man. Am J Hum Genet. 2012 Mar 9;90(3): 457-66. doi: 10.1016/j.ajhg.2012.01.018. Epub 2012 Feb 16.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22341972
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3309187/
- Tuschl K, Mills PB, Parsons H, Malone M, Fowler D, Bitner-Glindzicz M, Clayton PT. Hepatic cirrhosis, dystonia, polycythaemia and hypermanganesaemia--a new metabolic disorder. J Inherit Metab Dis. 2008 Apr;31(2):151-63. doi: 10.1007/s10545-008-0813-1. Epub 2008 Apr 4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18392750

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